# Table of Contents

## Main Topics
- Introduction ............................................. 2
- Institute Representatives .............................. 4
- A Brief History of the IMG ............................. 6
- IMG and Its Surroundings ............................... 7
- Research Groups ......................................... 8
- Services .................................................. 54
- Council of the IMG ....................................... 76
- Supervisory Board ....................................... 77
- Publications 2009-2010 .................................. 78
- Seminar Speakers 2009 ................................... 84
- Seminar Speakers 2010 ................................... 86
- Highlights of 2009-2010 ................................. 88
- Diploma Theses 2009 ...................................... 92
- Diploma Theses 2010 ...................................... 93
- PhD Theses 2009 .......................................... 94
- PhD Theses 2010 .......................................... 95
- Teaching (Semestral Courses) ......................... 96
- Our Location ............................................. 98
- Impressum ............................................... 100

## Research Groups
- Ladislav Anděra ........................... 8
- Jiří Bartek ........................................ 10
- Petr Bartůněk .................................. 12
- Jaroslav Blahoš ............................... 14
- Pavel Dráber .................................. 16
- Petr Dráber ..................................... 18
- Michal Dvořák .................................. 20
- Dominik Filipp .................................. 22
- Jiří Forejt ....................................... 24
- Jiří Hejnar ....................................... 26
- Vladimír Holáň .................................. 28
- Václav Hořejší .................................. 30
- Pavel Hozák ...................................... 32
- Pavel Janščák .................................. 34
- Vladimír Kořínek .................................. 36
- Zbyněk Kozmík .................................. 38
- Marie Lipoldová .................................. 40
- Milan Reiniš ...................................... 42
- Pavlína Řezáčová .................................. 44
- Radislav Sedláček .................................. 46
- David Staněk ...................................... 48
- Petr Svoboda ...................................... 50
- Čestmír Vlček ...................................... 52

## Information Technologies
- Information Technologies .......................... 54
  - Information Technologies .......................... 54
- Genomics and Bioinformatics ...................... 56
- Monoclonal Antibodies and Cryobank .............. 58
- Flow Cytometry and Light Microscopy .............. 60
- Media and Glass Washing .......................... 62
- Transgenic Unit .................................... 64
- Animal Facility (Mice) .............................. 66
- Animal Facility (Chicken) ......................... 68
- Building Maintenance ................................ 70
- Office of the Director .............................. 72
- Finances and Administration ....................... 73
- BIOCEV Division .................................. 74
Introduction

The period 2009-10 was rather eventful for IMG, as well as for the entire Academy of Sciences (AS) – partly due to the economic crisis generally, but mainly because of incompetent decisions made by the Council for Research, Development and Innovations of the Czech Government, which threatened to bring extremely serious consequences for the AS future. Fortunately, the AS employees demonstrated very strong opposition and in their protests received substantial support also from the public and from journalists. Many of us, unfortunately, lost hundreds of hours of valuable time in these “battles”. Despite this, I believe that all this effort was not in vain and that all will come right in the end. I was especially pleased by the active interest of young researchers (namely students) of the platform “Science Alive”.

In the past two years we were successful in what is our raison d’être – good science. We again published a number of scientific reports in peer-reviewed international scientific journals; we transferred a number of practically applicable products to our partner spin-off companies.

Of high importance for scientific life at our Institute was the organization of many scientific seminars and lectures given by our researchers and our guests. Our new conference hall (since January 2009 bearing the name “Milan Hašek Auditorium” in honour of Milan Hašek, the founder of our Institute) hosted several international conferences, some also organized by other AS institutes from the campus. I would like to mention the especially successful “EMBO Workshop on Mitochondria, Apoptosis and Cancer” held in October 2009, “Centennial Retrovirus Meeting” (May 2010), “The Second European Chemical Biology Symposium” (May 2010), “EMBO Young Scientists Forum” (June 2010) and “52nd Symposium of the Society for Histochemistry” (September 2010).

We completed the reconstruction of the animal facility for non-mouse models (mainly chicken), as well as the construction of a kindergarten and gym adjacent to our main building that will serve also our colleagues from other institutes of the campus.

We started the first phase of reconstruction of our chicken breeding facility in Koleč.

It is gratifying that our researchers repeatedly obtain rich and prestigious local and international grants to support their experiments aimed at discovering the still-so-many secrets of cells and tissues that decide about our health or disease.

At present, 23 research groups of the Institute are dealing with the topics covering molecular and cellular immunology, molecular and cellular oncology, cell biology of the nucleus, cytoskeleton, functional genomics and bioinformatics, study of oncogenes, molecular biology of development, structural biology and mechanisms of receptor signalling. An essential part of our Institute is represented by 95 doctoral students and 31 undergraduate students. A number of our scientists also act as university teachers (e.g. eight as professors and nine as associate professors).
Although we consider basic research as the highest priority, we are happy that some “by-products” of our basic research have practical importance. We are collaborating with several prospering biotech spin-off companies that have been born at the Institute in recent years.

In 2009-10, the Institute scientists were again authors or co-authors of publications in a number of prestigious international journals [e.g. Nature, Science, Molecular and Cellular Proteomics, Nucleic Acids Research, Human Molecular Genetics, Cancer Research, Blood, PLoS Pathogens, Cancer Cell, Current Biology, EMBO Reports, Journal of Cell Biology, Journal of Immunology, Oncogene, Cellular and Molecular Life Sciences, Journal of Cell Science, EMBO Journal, Journal of Virology, Nature Protocols].

The high standing of the Institute researchers is testified by awards and prizes; in 2009 Jiří Forejt was honoured with the Prize of the Minister of Education, Youth and Sports for outstanding results in research, experimental development and innovations for 2009: the team of Jiří Forejt laboratory [Zdeněk Trachtulec, Soňa Gregorová, Petr Jansa, David Homolka, Ondřej Mihola] was awarded the Prize of the Academy of Sciences of the Czech Republic; Ondřej Ballek obtained the Prize for the best diploma thesis awarded by the Dean of Charles University, Prague; Daniel Smrž [and the laboratory of Petr Dráber] received the Prize of the Czech Immunological Society for the best paper by a young immunologist in 2008; Petr Heneberg obtained the Bolzano Award awarded by the Rector of Charles University; Václav Pačes received the Prize of the Economia publishing house; Václav Hořejší was honoured with The Sir Hans Krebs Lecture and Medal awarded by FEBS; Daniel Smrž obtained the Award of the Czech Society for Analytical Cytology; Jiří Bartek was awarded The Shay Shacknai Prize for Cancer Research by the Hebrew University of Jerusalem, and the Medal of the Faculty of Medicine, Charles University. In 2010 Jan Svoboda was honoured with the National Prize of the Czech Government “Česká hlava” [Czech Brains]; Martina Huranová obtained from the Hlávka Foundation the Josef Hlávka Award for the best University students and graduates; Ondřej Mihola received the Arnold Beckman Prize for the best publication in the field of Genetics from Beckman Coulter CR and the Czech Society for Biochemistry and Molecular Biology; Václav Pačes was awarded the Medal of Emil Votoček by the Institute of Chemical Technology, Prague; Ondřej Mihola obtained the Scopus Award for year 2009 awarded by the prominent scientific publisher Elsevier BV; Jiří Bartek received The Neuron 2010 for life-long merits in medicine awarded by Karel Janeček Foundation.

Despite the potential funding problems, the development of our Institute complex is continuing successfully and I believe we can look forward to an exciting future.

Václav Hořejší
Director
Václav Hořejší
Director

Petr Dráber
Deputy Director

Jiří Špička
Deputy Director for Economy

Jan Rajnoch
Deputy Director for BIOCEV Project Implementation
Miroslav Flieger  
Member of the Academy Council of the ASCR  
Chairman of the Supervisory Board

Jiří Forejt  
Chairman of the Institute Council

Šárka Takáčová  
Institute Secretary

Institute Representatives
The Institute of Molecular Genetics, Academy of Sciences of the Czech Republic (IMG), is located on the southern outskirts of Prague, capital of the Czech Republic.

The history of the Institute started in 1953 with the establishment of the Department of Experimental Biology and Genetics of the Institute of Biology of the Czechoslovak Academy of Sciences, headed since then by Milan Hašek, co-discoverer of immunological tolerance. In 1961, the Department was transformed into the Institute of Experimental Biology and Genetics (IEBG), with Milan Hašek as its Director until 1970. The sixties of the last century were the “golden age” of the Institute, represented besides Hašek e.g. by Pavol and Juraj Iványi, Jan Klein, Jan Svoboda, etc. The end of the “Prague Spring” after August 1968 closed this famous era – many promising young scientists had emigrated (and were very successful at their new institutions abroad). In 1977, IEBG was re-organized and renamed Institute of Molecular Genetics of the Czechoslovak Academy of Sciences [IMG]; Josef Říman was appointed its Director. Among the achievements of the otherwise difficult seventies and eighties were co-discovery of reverse transcriptase (J. Říman), discovery of virogeny (J. Svoboda) or sequencing of one of the first viral genomes [V. Pačes]. After 1989, the Institute was headed by Jan Svoboda (1991-1999), Václav Pačes (1999-2005) and Václav Hořejší (2005-present). In the period 1964-2006, the Institute was divided between two distant locations. After completion of a modern new building for IMG in 2007, both parts moved together and the new premises are now hosting more than 350 employees and students.
The Prague-Krč Campus of Biomedical Institutes of the Academy of Sciences

IMG is located on the Krč campus also hosting the Institute of Microbiology, Institute of Physiology, Institute of Experimental Medicine, Institute of Biotechnology and part of the Institute of Animal Physiology and Genetics, in total over 1200 researchers and students. In close proximity to the site is also located the Institute of Clinical and Experimental Medicine (IKEM) and Thomayer Hospital. The campus lies near a major natural park (Krč forest), and is easily reachable by car or public transportation.

Prague – A City of History, Culture and Science

Situated on the Vltava (Moldau) river Prague has been the political, cultural, and economic centre of the Czech state for over 1000 years. The city is home to nearly 1.3 million people. Prague is widely considered to be one of the most beautiful cities in Europe and belongs to the most visited cities on the continent. Since 1992, the historic centre of Prague has been included in the UNESCO list of World Heritage Sites. Prague also has a long-standing tradition in science. Founded in 1348, Charles University is the oldest University in Central Europe. At present, Prague is the seat of eight public Universities, the student population being more than 100,000. There are also 36 institutes of the Academy of Sciences and a number of other research institutions.
Laboratory of Cell Signalling and Apoptosis

Death receptors, TRAIL, Daxx, cancer, cell death

Ladislav Anděra
ladislav.andera@img.cas.cz

Our group is interested in deciphering the signalling pathways leading to programmed death of cancer cells including cancer stem cells and uncovering mechanisms participating in regulation of these pathways. In our major focus stands TRAIL [TNFα-Related Apoptosis Inducing Ligand], a ligand from the TNFα family capable of inducing apoptosis of a number of transformed cells and not being harmful to the normal ones. TRAIL-induced apoptosis of sensitive cells is triggered by its interaction with TRAIL-R1/DR4 and/or TRAIL-R2/DR5. These receptors contain an α-helical protein–protein interaction domain called the death domain and belong together with Fas/CD95 or TNFR1 to the subfamily of TNFR receptors named "death receptors". We analyse several aspects of TRAIL's biological activities such as the role of endocytosis in TRAIL ligand-receptor[s] Death-Inducing Signalling Complex (DISC) formation and activation, TRAIL signalling in human embryonic stem cells (hESCs) and from them derived somatic progenitors or the effect of overexpressed/activated oncogenes such as c-Myc on TRAIL-induced apoptosis. In our collaborative projects we uncovered two novel drugs sensitizing resistant cancer cells to TRAIL-induced apoptosis and participated in the analysis of multiple aspects of TRAIL-signalling in leukaemia and colon carcinoma cells. In our other death receptors-related project we characterize molecular and expression patterns of the Death Receptor 6 (DR6), which can participate in the regulation of T- and B-cell activation. We have discovered that posttranslational modifications of DR6 can affect the cellular localization of this highly glycosylated and palmitoylated receptor, and we currently analyse regulation of DR6 expression in T cells. Part of our group also analyses molecular and functional properties of the for embryonic development essential adapter protein Daxx. Daxx apparently participates in stress- and Fas/CD95-triggered apoptosis, and it is also involved in the regulation of multiple other processes such as transcription or cell cycle. We currently characterize functional consequences of its interaction with several new Daxx-binding proteins such as Brg1 or BAP1 and in collaboration we assess the role of Daxx in DNA damage response.

From left:
Jarmila Stremenová, PhD / Postdoc (since 2010)
Simona Benešová / Technician
Liina Rankel, MSc / PhD (since 2010)
Ladislav Anděra, PhD / Head of Laboratory
Jan Bražina, MSc / PhD Student
Jan Švadlenka, MSc / PhD Student
Náda Hradilová / Diploma Student (since 2009)
Michal Koc, PhD / Postdoc
Martin Klíma, MSc / PhD Student

Not on the picture:
Lenka Beranová, MSc / PhD Student
Lukáš Dermát, PhD / Phd (until 2009)
Vladimíra Horová, MSc / PhD Student
Leonard Nevařil, MSc / PhD Student (until 2010)
Šárka Šímová, PhD / Secretary
Realization of complex tasks of living organisms depends on information stored in DNA of their genomes. The loss of this information due to endogenous and exogenous physicochemical damage of DNA results in disintegration of homeostasis at the cellular and organism level manifested as diseases including cancer and ageing. Several tightly orchestrated mechanisms take care to preserve the intactness of genetic information by preventing and repairing DNA damage. Our research is centered on cellular responses [termed collectively DNA damage response; DDR] to DNA double-strand breaks, presumably the most deleterious lesions affecting DNA. Cells with unhealed chromosomal breaks are mostly prevented from cell division due to activated DNA damage cell cycle checkpoints; however, following unscheduled cell division, unrepaired breaks result in chromosomal instability with accompanying changes in gene dosage – the driving force of malignant transformation.

Specifically we focus on 1) posttranslational modifications [phosphorylation, ubiquitylation, sumoylation and acetylation] of key players involved in sensing and transmitting signals from DNA breaks to cellular effectors responsible for activation of cell cycle checkpoints and repair; 2) mechanisms of DNA damage cell cycle checkpoint recovery after successful DNA repair; 3) mechanisms of cellular response to chronic irreparable DNA damage manifested as irreversible cell cycle arrest [cellular senescence]; and 4) role of DNA damage-activated expression of secreted factors [cytokines] in autocrine/paracrine signalling and intercellular communication, and 5) impact of the above mechanisms on cancer and ageing. Recently, we have characterized cytokine expression in chemotherapeutic drug-induced cellular senescence and the role of activated interferon JAK/STAT signalling pathway in autocrine/paracrine induction of tumour suppressors such as PML, STAT1 and IRF-1. We have found that normal and tumour human cells escaping acute intoxication with specific bacterial toxin, cytotoxial distending toxin, undergo irreversible cell cycle arrest with all hallmarks of cellular senescence including irreparable chromosomal damage and cytokine expression. In collaboration with R. Medema group [University of Utrecht, Netherlands], we have investigated the role of Wip1 phosphatase in dephosphorylation of DNA damage-associated modification of histone protein H2AX and in DNA damage checkpoint recovery. Currently, we are performing high-throughput siRNA-based phenotypic screening to discover factors involved in posttranslational modifications of DDR components and functional characterization of positive ‘hits’.

Research groups


In collaboration with R. Medema group (University of Utrecht, Netherlands), we have investigated the role of Wip1 phosphatase in dephosphorylation of DNA damage-associated modification of histone protein H2AX and in DNA damage checkpoint recovery. Currently, we are performing high-throughput siRNA-based phenotypic screening to discover factors involved in posttranslational modifications of DDR components and functional characterization of positive ‘hits’.

Laboratory of Genome Integrity

DNA damage response, cell cycle, oncogenic transformation, cellular senescence, ageing

Jiří Bartek
jiri.bartek@img.cas.cz
From left:
Libor Macůrek, MD, PhD / Research Fellow (since 2010)
Hana Havlíčková, PhD / Postdoc
Soňa Hubáčková, MSc / PhD Student
Pavel Moudrý, MSc / PhD Student
Jiří Barták, Prof, MD, PhD / Head of Laboratory
Jan Reneta / Diploma Student (since 2009)
Markéta Vančurová, MSc / PhD Student (since 2010)

Not on the picture:
Markéta Černohorská / Diploma Student [until 2009]
Pavína Dušková / Diploma Student [until 2009]
Zdeněk Hodny, MD, PhD / Deputy Head
Ivona Kopová / Diploma Student [until 2009]
Martin Košař, MSc / PhD Student
Katerina Krejčková, MSc / Research Assistant
Zora Nováková, MSc / PhD Student [until 2010]
Laboratory of Cell Differentiation

Chemical genetics, haematopoietic and neural cell differentiation, signalling pathways, nuclear receptors

Petr Bartůněk
petr.bartunek@img.cas.cz

The main interest of the laboratory lies in the molecular mechanism of cell fate determination. In the lab we have established in vitro systems to study the self-renewal and differentiation of haematopoietic, neural and mesenchymal stem cells. We use growth factors and small molecules as tools to manipulate these systems. More recently, we have initiated more systematic search for such tools using chemical biology/genetics approaches.

Nuclear receptors function as ligand-dependent transcription factors to regulate gene transcription in response to specific physiological stimuli such as steroids, retinoids, thyroid hormone and vitamin D. Thyroid hormone receptors, activated in response to thyroid hormone (T3), are known to modulate the level of serum cholesterol via complex regulatory pathways. By screening for T3-regulated genes we have identified Disp3, a sterol-sensing domain-containing protein that is related to the Dispatched family of proteins. DISP3 is predominantly expressed in specific cell types of the brain, retina and testis and localizes within the endoplasmic reticulum, and was found to co-localize with cholestrol. Ectopic expression of DISP3 in fibroblasts resulted in elevated cholesterol levels combined with an altered cholesterol distribution. We proposed that DISP3 represents a new molecular link between thyroid hormone and cholesterol metabolism in the brain (Zikova et al. 2009). Moreover, we have identified two neural stem cell lines that highly express Disp3. Disp3 expression is positively regulated by T3 treatment, and upon differentiation the level of Disp3 dramatically changes, suggesting that Disp3 may modulate self-renewal or differentiation. Brain tumours such as medulloblastoma are believed to arise from neural precursor cells. Analysis of a small number of primary human tumours revealed very high expression of Disp3, suggesting an important role for this protein in their pathogenesis. We have performed RNAi and overexpression studies and found out that Disp3 is able to modulate the cell fate of neural stem cells and their progeny.

We have also identified, cloned and characterized the first non-mammalian Tpo, chicken thrombopoietin, and its receptor c-Mpl. Discovery of chicken Tpo and c-Mpl will greatly facilitate future studies regarding thrombocytic differentiation and haematopoietic stem cell development. Moreover, we have introduced an experimental model of chicken bi-potent thrombo/erythropoietic progenitors that can be used to identify key regulators of cell fate determination (Bartunek et al. 2008). In addition, we have extended our studies to vertebrate hematopoietic development by introducing a new model organism in our laboratory – the zebrafish – and we established the first ex vivo cultures of haematopoietic cells (Stachura et al. 2009).

Research groups

- Ministry of Education, Youth and Sports of the Czech Republic, LC06077 – Centre of Chemical Genetics, 2006-2010, P. Bartůněk
- FP7 EU, 261861 EU-OPENSCREEN – European Infrastructure of Open Screening Platforms for Chemical Biology, 2010-2013, P. Bartůněk
- GA CR, GA310/08/0878 – The role of the cells prion protein in erytroidnic differentiation: possible link to peripheral pathogenesis of prion diseases, 2008-2012, P. Bartůněk
- GA CR, GAP305/10/0953 – New regulators of megakaryocyte and erythroid lineage commitment, 2010-2013, P. Bartůněk

From left:
- Michaela Marešová, MSc / Research Assistant (until 2009)
- Ondřej Svoboda, MSc / PhD Student
- Jana Konrířová, MSc / PhD Student (since 2010)
- David Sedlák, MSc / PhD Student
- Jana Bartůňková, MD / Research Assistant
- Martina Zíková, PhD / Research Fellow
- Petr Bartůněk, PhD / Head of Laboratory
- Jindřich Jindřich, Assoc Prof, PhD / Research Fellow
- Antonio Pombinho, MSc / PhD Student
- Jana Oltová / Diploma Student (since 2009)

Not on the picture:
- Alicia Corlett, PhD / Postdoc (until 2010)
- Lucie Gráfová, MSc / PhD Student (09/2009 - 09/2010)
- Eva Mašínová, MSc / Research Assistant
- Michael-Robin Witt, PhD / Research Fellow (until 2009)
- Petra Žáková / Technician (until 2010)
In mammalian brain the major excitatory neurotransmitter glutamate activates two types of receptors: ligand-operated ion channels (NMDA, AMPA and kainate receptors) and G protein-coupled receptors [GPCRs]. There are eight genes that code for the metabotropic glutamate [mGlu] receptors in mammals. These receptors diverge in location within brain regions and cellular compartments and have distinct functions. As such, they constitute possible promising targets for treatment of several neurological diseases. Our research is focused on the structure-function relationships of these receptors and molecular machinery that regulates their signalling properties. The mGlu receptors belong to family C GPCRs and are traditionally viewed as composed of two identical subunits. Using the mutagenesis approach combined with a functional expression system we showed that within their homodimeric complexes only one HD reaches active state. Our recent data using dynamic FRET approach are in accord with this notion. The activation process of these family 3 GPCRs is thus asymmetrical. Recent data suggest that the mGluRs can also form heterodimers. We published data suggesting that heterodimerization between distinct splice variants of the mGlu1 receptor, the mGluR1a and mGluR1b, results in novel receptor complexes with altered function and trafficking properties in transfected heterologous cells. Now we aim at revealing the situation in brain using a set of splice variant-specific antibodies we developed.

The cannabinoid receptor project is focused on regulation of signalling of the CB1 receptor. It is approached by molecular biology techniques combined with biochemical tools including yeast two-hybrid screen. Currently, several hits obtained by the latter technique are being analysed. One highly promising lead is investigated in deep detail. The mechanism of regulation of cell-surface stability of the CB1 receptor by endocytosis machinery proteins shows possible novel player(s). The mechanism of internalization of the CB1 receptor and its regulation is therefore currently under heavy investigation in our lab.

Fig. 1. Splicing of rat metabotropic glutamate receptor 1 (mGluR1) gene results in expression of long and short forms. Following the heptahelical domain and short sequence including RRKK motive (Endoplasmic Reticulum retention signal), the long form mGluR1a has a unique sequence of 312 aa, short forms are termed mGluR1b and d. The mGluR1b unique sequence is 19 aa long following the splicing site.

Fig. 2. For immunocytochemistry cells were transfected with HA-mGluR1a and stained with monoclonal anti-HA antibodies (secondary antibodies labelled with FITC) and our N14 antibodies (secondary anti-rabbit antibodies labelled with Cy3) and detected with secondary antibodies (FITC, Cy3, respectively). Their patterns confirm specificity of the novel antibodies by overlap of corresponding anti-tag antibodies and staining with the subunit-specific sera. Bar equals to 10 µm in vivo.
The long-term research programme of the laboratory has been focused on studying the structure-function relationships of microtubule (MT) proteins and their interactions with other cytoskeletal elements in cells under normal and pathological conditions. The organization of dynamic MT networks is controlled by microtubule organizing centres (MTOCs). One of the key components of MTOCs is γ-tubulin, which is necessary for nucleation of MT. Current work focuses on the understanding of the modulation of MT properties by signal transduction molecules, the function of γ-tubulin forms, and molecular and functional characterization of regulators of microtubule nucleation. To address these questions, techniques of molecular biology, biochemistry and immunology are being used, as well as a variety of microscopic techniques, including live cell imaging using TIRF microscopy. Our results demonstrate that rearrangement of microtubules in activated mast cells depends on activity of the stromal interacting protein 1 (STIM1) and that Ca²⁺ plays an important role in the formation of microtubule protrusions in activated cells. We have also shown that non-receptor protein tyrosine kinases play an important role in MT nucleation. We have demonstrated that prediction of epitope exposure on microtubules by means of homology modelling combined with site-directed antibodies can contribute to better understanding of the interactions of microtubules with associated proteins. Finally, we have shown that ectopic expression of tubulins may represent a novel marker in pathobiology of glioblastoma multiforme, the most common and deadliest form of primary brain cancers.

From left:
Eduarda Dráberová, PhD / Research Fellow
Zuzana Hájková / Diploma Student
Markéta Čermářová, MSc / PhD Student
Věra Richterová, MSc / Research Assistant
Ladislav Cupák / Technician
Stanislav Víncal, MSc / PhD Student
Irena Michalová / Technician
Tetyana Sulimenko, MSc / Research Assistant
Vadym Sulimenko, PhD / Research Fellow
Jan Pales / Diploma Student
Pavel Dráber, Asoc Prof, PhD / Head of Laboratory

Not on the picture:
Karel Beránek / Diploma Student
Vladimíra Marková, PhD / Research Assistant [maternity leave]
Barbora Hořejší, MSc / PhD Student [maternity leave]
The plasma membrane possesses a variety of molecules [mainly proteins and lipids] that are involved in such important cellular functions as cell migration, adhesion and signalling. Our recent studies have been focused on understanding the roles of selected plasma membrane–associated components at initial stages of mast cell activation. We analyzed functions of the transmembrane adaptor protein NTAL and the roles of protein tyrosine phosphatases [PTPs] at early stages of mast cell signalling induced via the high-affinity IgE receptor (FcεRI) or c-kit. We found that mast cells isolated from NTAL-deficient cells exhibited reduced spreading on fibronectin, enhanced filamensous actin depolymerization and enhanced migration towards antigen when compared to wild-type cells. To understand the molecular basis of these phenomena, we examined activities of two small GTPases, Rac and Rho, important regulators of actin polymerization. Stimulation of the cells via FcεRI enhanced activity of Rac[1,2,3] in both NTAL-deficient and wild-type cells. In contrast, the RhoA activity decreased and this trend was much faster and more extensive in NTAL-deficient cells, indicating a positive regulatory role of NTAL in the recovery of RhoA activity. After restoring NTAL into NTAL-deficient cells, both spreading and actin responses were rescued. Thus, our studies showed for the first time that NTAL has a crucial role in signalling, via RhoA, to the mast cell cytoskeleton.

The earliest known biochemical step in FcεRI-activated cells is tyrosine phosphorylation of the receptor subunits by Src family kinase Lyn. However, the exact molecular mechanism of this phosphorylation step is incompletely understood. We therefore tested our hypothesis that changes in the activity and/or topography of protein tyrosine phosphatases could play a major role in the FcεRI triggering. We found that exposure of mast cells to PTP inhibitors induced phosphorylation of the FcεRI subunits, similarly as FcεRI triggering. Interestingly, and in sharp contrast to antigen–induced activation, the inhibitors had no effect on association of FcεRI with detergent-resistant membranes and their topography in the plasma membrane. In cells stimulated with antigen or the inhibitors, enhanced oxidation of active site cysteine of several PTPs was detected. Unexpectedly, most of oxidized phosphatases bound to the plasma membrane were associated with the actin cytoskeleton. Based on these and other data we proposed that down–regulation of enzymatic activity of PTPs and/or changes in their accessibility to the substrates play a key role in initial tyrosine phosphorylation of the FcεRI and other multichain immune receptors.

**Research groups**


The recent research efforts of the group focus on genes and molecular mechanisms involved in 1) malignant transformation of haematopoietic cells, melanocytes, nephrogenic blastema, liver and lung cells; 2) metastasis and interactions between a tumour and its microenvironment; 3) fate determination in multipotent neural cells and differentiation of myogenic precursors; 4) apoptosis induced by photoactivation of specific porphyrins and development of porphyrin derivatives for potential use in photodynamic therapy. In studies on cell fate determination, differentiation and malignant transformation of haematopoietic and neural cells [collaboration with the Institute of Anatomy, Prague], myb genes are used as tools to modulate development of avian cells and tissues. In studies on genes involved in the formation of kidney, liver and lung tumours in chicks, insertional mutagenesis by MAV retroviruses is exploited. Genes of the egr family serve as tools to affect epithelial and mesenchymal cell phenotypes and metastatic potential of experimental tumours. Porphyrin derivatives synthesized by the cooperating group [Institute of Chemical Technology, Prague] are used for experiments with targeted drug delivery and induction of cell death in cancer cells and tissues.
The group was established in the summer of 2007. The central theme of our research is the molecular and functional characterization of innate immune mechanisms involved in the process of sterile inflammation, developmental tissue remodelling and chronic inflammatory diseases. Our main effort is focused on Toll-like receptors and other TIR domain-containing immune-related proteins and their role in the early embryogenesis. Data accumulated so far point to the spatially and temporarily regulated expression of TLRs on embryonal phagocytes, suggesting their involvement in sterile inflammation during early development. The characterization of a complete set of innate immune receptors (IIRs) expressed on embryonal phagocytes and evaluation of their signalling competence, together with elucidation of the nature of endogenous ligands for these IIRs represent our main objectives. Further, the cDNA microarray analyses performed on embryonal phagocytes revealed cell-specific expression of several uncharacterized molecules that could play an essential role in the processes supporting embryonal homeostasis. In collaboration with our partner laboratories we have also characterized immunomodulatory activities of enzymatically synthesized oligofuranosides (1). Recent data indicate their robust adjuvant properties with prophylactic and therapeutic potential. Our research is also geared towards the understanding of the contribution of cellular and humoral innate immune factors to the onset and maintenance of autoimmune processes. In collaboration with clinical laboratories we were able to demonstrate increased levels of defensin expression in recently diagnosed patients suffering from autoimmune diseases. Our main mission here is to characterize novel predictive biomarkers suitable for diagnosis of these diseases in the pre-clinical phase of their development. In this context we have also characterized the distribution and tissue-specific functions of alpha-defensins in rat experimental models (2). We also continue in our effort to understand very early biochemical events leading to activation of T cells. Our previous study showed that the critical event in this process is the translocation and subsequent enrichment of kinase active Lck in lipid rafts (LR) (3). While other regulatory proteins are also recruited to LR upon T-cell activation, the mechanism of these translocations, indispensable for T-cell activation, is largely unknown. The main goal of this line of research is the characterization of the molecular mechanism and its structural elements underpinning the recruitment of Lck and other signalling molecules to LR. In addition, we provide technical and knowledge support for exploration of several molecular approaches in unrelated projects (4, 5).

The group was established in the summer of 2007. The central theme of our research is the molecular and functional characterization of innate immune mechanisms involved in the process of sterile inflammation, developmental tissue remodelling and chronic inflammatory diseases. Our main effort is focused on Toll-like receptors and other TIR domain-containing immune-related proteins and their role in the early embryogenesis. Data accumulated so far point to the spatially and temporarily regulated expression of TLRs on embryonal phagocytes, suggesting their involvement in sterile inflammation during early development. The characterization of a complete set of innate immune receptors (IIRs) expressed on embryonal phagocytes and evaluation of their signalling competence, together with elucidation of the nature of endogenous ligands for these IIRs represent our main objectives. Further, the cDNA microarray analyses performed on embryonal phagocytes revealed cell-specific expression of several uncharacterized molecules that could play an essential role in the processes supporting embryonal homeostasis. In collaboration with our partner laboratories we have also characterized immunomodulatory activities of enzymatically synthesized oligofuranosides (1). Recent data indicate their robust adjuvant properties with prophylactic and therapeutic potential. Our research is also geared towards the understanding of the contribution of cellular and humoral innate immune factors to the onset and maintenance of autoimmune processes. In collaboration with clinical laboratories we were able to demonstrate increased levels of defensin expression in recently diagnosed patients suffering from autoimmune diseases. Our main mission here is to characterize novel predictive biomarkers suitable for diagnosis of these diseases in the pre-clinical phase of their development. In this context we have also characterized the distribution and tissue-specific functions of alpha-defensins in rat experimental models (2). We also continue in our effort to understand very early biochemical events leading to activation of T cells. Our previous study showed that the critical event in this process is the translocation and subsequent enrichment of kinase active Lck in lipid rafts (LR) (3). While other regulatory proteins are also recruited to LR upon T-cell activation, the mechanism of these translocations, indispensable for T-cell activation, is largely unknown. The main goal of this line of research is the characterization of the molecular mechanism and its structural elements underpinning the recruitment of Lck and other signalling molecules to LR. In addition, we provide technical and knowledge support for exploration of several molecular approaches in unrelated projects (4, 5).

The group was established in the summer of 2007. The central theme of our research is the molecular and functional characterization of innate immune mechanisms involved in the process of sterile inflammation, developmental tissue remodelling and chronic inflammatory diseases. Our main effort is focused on Toll-like receptors and other TIR domain-containing immune-related proteins and their role in the early embryogenesis. Data accumulated so far point to the spatially and temporarily regulated expression of TLRs on embryonal phagocytes, suggesting their involvement in sterile inflammation during early development. The characterization of a complete set of innate immune receptors (IIRs) expressed on embryonal phagocytes and evaluation of their signalling competence, together with elucidation of the nature of endogenous ligands for these IIRs represent our main objectives. Further, the cDNA microarray analyses performed on embryonal phagocytes revealed cell-specific expression of several uncharacterized molecules that could play an essential role in the processes supporting embryonal homeostasis. In collaboration with our partner laboratories we have also characterized immunomodulatory activities of enzymatically synthesized oligofuranosides (1). Recent data indicate their robust adjuvant properties with prophylactic and therapeutic potential. Our research is also geared towards the understanding of the contribution of cellular and humoral innate immune factors to the onset and maintenance of autoimmune processes. In collaboration with clinical laboratories we were able to demonstrate increased levels of defensin expression in recently diagnosed patients suffering from autoimmune diseases. Our main mission here is to characterize novel predictive biomarkers suitable for diagnosis of these diseases in the pre-clinical phase of their development. In this context we have also characterized the distribution and tissue-specific functions of alpha-defensins in rat experimental models (2). We also continue in our effort to understand very early biochemical events leading to activation of T cells. Our previous study showed that the critical event in this process is the translocation and subsequent enrichment of kinase active Lck in lipid rafts (LR) (3). While other regulatory proteins are also recruited to LR upon T-cell activation, the mechanism of these translocations, indispensable for T-cell activation, is largely unknown. The main goal of this line of research is the characterization of the molecular mechanism and its structural elements underpinning the recruitment of Lck and other signalling molecules to LR. In addition, we provide technical and knowledge support for exploration of several molecular approaches in unrelated projects (4, 5).
Genetic architecture of hybrid male sterility between Mus m. musculus and Mus m. domesticus subspecies has been analysed on the model of PWD/Ph x C57BL/6 sterile male hybrids. The candidate genes were evaluated by transgenic rescue for the Hst1 locus and by positional cloning and expression profiling of sorted testicular cells for the Hstx1 and Hstx2 loci. We have identified the first vertebrate hybrid sterility locus, the mouse Hybrid sterility 1 (Hst1) with Prdm9 [Meisetz], encoding a meiotic histone H3 lysine-4 tri-methyltransferase. Positional cloning was confirmed by hybrid male infertility rescue by using the intact Prdm9 transgene in bacterial artificial chromosomes with the "fertility" Hst1 allele. Identification of the first vertebrate hybrid sterility gene reveals a role for epigenetics in speciation, and opens a window to a hybrid sterility gene network. We have established a new mouse model of human aneuploidy syndromes. The Ts43H segmental trisomy of proximal 30 MB of mouse chromosome 17 encompasses over 300 protein-coding genes. Chromosome substitution strains C57BL/6.PWD, recently constructed in our laboratory, are used for phenotype analysis in collaboration with The Jackson Laboratory, Bar Harbor, Maine, USA [Dr. K.L. Svenson] and for the genetics of gene expression and splicing in a systems genetics project with the Max-Planck-Institute for Molecular Genetics in Berlin [Prof. H. Lehrach]. We study meiotic X-chromosome inactivation by genome-wide expression profiling and by monitoring transcription profiles and histone modifications in meiotic and postmeiotic testicular cells of carriers of male-sterile autosomal rearrangements and in male-sterile inter-species hybrids.
Retroviruses interact with the host cells at multiple levels. They enter cells via specific receptors, integrate into the host genome, and use the cell transcription machinery to express their structural or enzymatically active proteins. Specific binding of retroviral envelope proteins to host cell receptors is the prerequisite for cell permissiveness to the infection. Retroviruses broaden their host range by mutations of the env gene, and vice versa, host cells develop resistance to retrovirus by mutations of genes encoding the specific receptors. We have described such an interesting semi-resistant phenotype in chicken line M and explained it by mutation of the receptor Tvb. Another defence mechanism used by the host cells is the inactivation of integrated invaders at the level of transcription via DNA methylation and modifications of adjacent histones. This was demonstrated in the case of HIV-1 latency, and inhibitors of DNA methyltransferases and histone deacetylases must be considered for HIV-1 eradication from the reservoir of long-lived, latently infected resting memory CD4+ T cells. Another example of epigenetic regulation is represented by endogenous retroviruses in the human genome. Fusogenic envelope glycoproteins encoded by two copies of HERVs are strictly placenta-specific and their expression in other tissues must be prevented by DNA methylation and histone methylation. Epigenetic silencing is, however, an obstacle in using retroviruses as vectors for gene transfer and transgenesis. We have improved ASLV-based retroviral vectors by insertion of core element from CpG island between promoter and enhancer, which increases their resistance to transcriptional silencing and ensures long-term expression of transduced genes. Finally, we have identified two genomic copies of porcine endogenous retroviruses as a potential risk factor in xenotransplantation of pig organs and tissues.
Transplantation of organ or transfer of stem cells often represents the only way to improve or even to rescue life. However, immunological rejection represents the major obstacle to further development of clinical transplantation. Therefore, deep knowledge of molecular and cellular mechanisms of the transplantation reaction is required. Using the model of immunological reaction to histocompatibility antigens we have focused on the study of activation and function of regulatory T cells in transplantation immunity and tolerance. On the model of orthotopic corneal and limbal transplantation we have analysed expression of genes for cytokines and other effector molecules during graft rejection and studied possibilities to prevent rejection of corneal and limbal grafts. Since successful treatment of damaged cornea requires transfer of limbal stem cells, we recently started to isolate, grow and characterize stem cells. We succeeded in isolating limbal and mesenchymal stem cells in the mouse and using them for the repair of damaged corneal epithelium. For the transfer of stem cells we use various types of nanofibre scaffolds, which represent optimal 3D matrices for stem cell growth. Well-established methods for monitoring the immune response enabled us, in co-operation with other laboratories, to study cytokine response in various experimental models of immunoregulation. The ultimate goal of our research is to get insights into the mechanisms of specific immune response, to isolate and transplant stem cells and to propose novel strategies for targeted immunoregulation.
From left:
Milada Chudíčková, MSc / PhD Student (since 2010)
Hana Kuthanová / Diploma Student (since 2009)
Jaroslava Krňáková / Technician
Vladimír Holáň, Assoc Prof, DSc / Head of Laboratory
Alena Zajícová, PhD / Research Fellow
Lucie Holáňová / Technician
Zdeněk Zadražil / Diploma Student (since 2010)
Eliška Svobodová, MSc / PhD Student
Kateřina Pokorná, MSc / PhD student
Jana Procházková, MSc / PhD Student
Peter Trošan, MSc/PhD Student (since 2009)
Magdaléna Krulová, PhD / Research Fellow

Not on the picture:
Helena Faltýsková / Diploma Student (until 2010)
Michaela Plešníková / Diploma Student (until 2009)
Kristýna Kadlecová / Diploma Student
Anna Lenčová, MD / PhD Student
In recent years a major topic of our laboratory has been signalling molecules present in membrane rafts, namely several transmembrane adaptor proteins discovered previously by us (PAG/Cbp, NTAL/LAB, LIME) and their involvement in immunoreceptor signalling. In 2009-2010 we worked on elucidation of the structure and function of an apparently novel type of "heavy" rafts, differing from the "classical" ones by higher protein-lipid ratio and containing a number of transmembrane proteins. We continued our studies on several novel raft-associated transmembrane adaptors (LST1A, PRR7, Nvl), targeting of protein tyrosine kinase Csk into various membrane compartments, on receptor phosphatase CD148, and collaborated on several studies concerning membrane rafts and their components. Furthermore, we produced a number of novel monoclonal antibodies as valuable research and potentially diagnostic tools, e.g. those to LARBE, CLIC 5, OPAL 1, DDIT4L.
From left:
Aleš Drobek, MSc / PhD Student (since 2010)
Pavel Otáhal, MD, PhD / Postdoc
Tomáš Brdička, PhD / Research Fellow
Barbora Dvořáková / Diploma Student (since 2010)
Karel Drbal, PhD / Research Fellow
Jana Pakorná / Technician
Ondřej Štěpánek, MSc / PhD Student
Pavla Angelisová, PhD / Research Fellow
Markéta Kucová / Technician (since 2009)
Pavel Dráber, MSc / PhD Student
Václav Hofejžl, Prof, PhD / Head of Laboratory

Not on the picture:
Lukáš Chiml, MSc / PhD Student (until 2009)
Matouš Hrdinka, MSc / PhD Student
Tereza Skopcová, Bc / Technician [maternity leave]
Tereza Gminda (Nováková), MSc / PhD Student
Supansa Pata, MSc / PhD Student (until 2010)
Pavel Pitule / Diploma Student (until 2010)
Lucie Sobětová / Technician
Jitka Solcová / Diploma Student (until 2010)
Eva Trnovcová / Secretary
Ivana Volfínková / Diploma Student (until 2010)
In diploid mammalian cells, some $6 \times 10^9$ base pairs of DNA fold as a nucleoprotein complex [i.e., chromatin] into higher-order arrays so as to fit in a nucleus measuring only 10 μm. The nucleus also contains machineries for transcription of genes and processing of RNA products, and for precise DNA replication, repair and recombination. Nuclear interior is therefore functionally highly compartmentalized, and the recent evidence points strongly to structure-related regulation of nuclear functions – however, the mechanisms forming the 3D-structure of the nucleus are still mostly obscure. We therefore employ a multi-disciplinary approach in order to study nuclear functions in relation to the higher-order nuclear structures, e.g., nuclear bodies, the nucleus, and the nucleoskeleton. Our research concentrates on: (1) the relationship between nuclear compartmentalization and regulation of gene expression, (2) structure, dynamics, and function of the nucleoskeleton, which might direct nuclear compartmentalization, (3) functions of nuclear myosin I and actin in transcription and gene expression, (4) development of new microscopy methods for ultrastructural studies.
Pavel Kříž / Technician
Lenka Příšlová / Secretary
Ivanka Nováková / Technician
Pavel Marášek, MSc / PhD Student
Sukriye Yildirim, MSc / PhD Student
Margaryta Sobol, PhD / Research Fellow
Vladimir Kononenko, PhD / Research Fellow
Jana Romankova, MSc / Research Assistant [since 2009]
Pavel Hozák, Prof. CSc / Head of Laboratory
Tomáš Venit, MSc / PhD Student [since 2009]
Magdaléna Skalníková, PhD / Research Fellow [since 2009]
Anatoly Philimonenko, MSc / Research Assistant
Karel Janoušek / Technician

Not on the picture:
Enrique Castano, PhD / Research Fellow (until 2010)
Rastislav Dzijak, MSc / PhD Student
Jitka Fialková, PhD / Research Fellow (since 2010)
Jana Fukalová, PhD / PhD Student
Lenka Jarolímová, MSc / Research Assistant
Iva Jelínková / Technician
Michal Kahle, MD, PhD / Research Fellow (until 2009)
Alžběta Kalendová, MSc / PhD Student
Jakub Kukla / Diploma Student (until 2009)
Amirhossein Sharifzadeh, MSc / PhD Student (since 2010)
DNA damage is a frequent event in the life of a cell. Failure to repair DNA damage can lead to cell death, while inaccurate DNA repair can give rise to genomic instability, which promotes the onset of cancer in mammals. Proteins belonging to the RecQ family of DNA helicases play important roles in the maintenance of genomic stability in all kingdoms of life, which is highlighted by the finding of an association of inherited defects in three human RecQ helicases, namely BLM, WRN and RECQ4, with distinct autosomal recessive disorders characterized by genomic instability and cancer predisposition. The main goal of the research in our laboratory is to provide a clear understanding of the functions of these enzymes in mammalian cells. Our current studies focus on RECQ4, which is mutated in Rothmund-Thomson syndrome, a severe disorder manifested by photosensitivity, skeletal abnormalities, aneuploidy, chromosomal rearrangements and predisposition to osteosarcomas. A number of recent studies have demonstrated that RECQ4 is essential for the initiation of DNA replication. However, RECQ4 also accumulates at DNA double-strand breaks (DSBs) and interacts with the RAD51 recombinase that mediates homology search and strand exchange during DSB repair by homologous recombination (HR). Our aim is to explore the role of RECQ4 in DNA DSB repair. Although HR between sister chromatids provides the most accurate mechanism for repair of DSBs, it has to be tightly regulated, especially at the strand invasion step, to prevent recombination events between homologous sequences at different chromosomal loci, which can give rise to chromosomal rearrangements. A number of DNA helicases including FBH1 have been implicated in the regulation of HR, but the underlying mechanisms remain elusive. Another goal of the laboratory is to elucidate the mechanistic basis of the anti-recombinase function of FBH1.
From left:
Kamila Burdíková, MSc / PhD student
Igor Shevelev, PhD / Research Fellow
Jitka Šimandlová / Diploma Student
Pavel Jaměček, PhD / Head of Laboratory
Polina Zjablovskaja, MSc / PhD student (since 2010)
Irina Sheveleva, MSc / Research Assistant
Ondřej Žítek / Diploma Student

Not on the picture:
Václav Urban, MSc / PhD student
The majority of tissues in the adult organism contain a population of tissue-specific stem cells. These multipotent cells are involved in homeostatic self-renewal and tissue repair processes. The biology of the stem cells is driven by a limited set of signalling cascades. The deregulation of these cascades can ultimately lead to the cellular transformation and formation of tumours. This clearly indicates the connection between the stem cell physiology and cancer. The scientific goal of the laboratory is to elucidate molecular mechanisms influencing behaviour of normal and diseased intestinal epithelial cells. Since the fate of these cells is determined by the so-called Wnt signalling pathway, our main focus is to find genes regulated by the Wnt pathway and/or encoding proteins directly involved in the signalling process. The important result in the current years was the identification of the HIC1 (Hypermethylated In Cancer 1) tumour suppressor as a novel modulator of the Wnt signalling cascade. Moreover, using various molecular biology approaches we discovered several other proteins (e.g. Dazap2 and Troy) that participate in Wnt signalling or act in downstream molecular events triggered by active Wnt signalling. Currently, the laboratory used the gene targeting technology in mouse embryonic stem cells to produce a novel mouse strain containing a so-called conditional allele of the Hic1 gene. Furthermore, we generated several “reporter” mice allowing lineage tracing experiments in mouse embryonic and adult tissues.


Laboratory of Cell and Developmental Biology
Colorectal cancer, Wnt signalling, TCF/LEF transcription factors, Hypermethylated in Cancer 1, HIC1

Vladimír Kořínek
vladimir.korinek@img.cas.cz
From left:
Eva Šloncová, MSc / Technician, Secretary
Bohumil Fafílek, MSc / PhD Student
Vendula Pospíchalová, MSc / PhD Student
Vladimír Kořínek, PhD / Head of Laboratory
Lucie Tůmová, MSc / PhD Student (since 2009)
Martina Vojtěchová, PhD / Research Fellow
Jolana Turečková, PhD / Research Fellow
Adéla Hlavatá / Diploma Student (since 2010)
Michaela Krausová, MSc / PhD Student

Not on the picture:
Lenka Doubravská, MSc / PhD Student (maternity leave)
Jan Lukáš, MSc / PhD Student (until 2009)
Petr Mazná, PhD / Postdoc (until 2010)
Jakub Novák / Diploma Student (until 2009)
Tomáš Valenta, PhD / Research Fellow (until 2009)
We are interested in the genetic basis of mammalian eye development. Our focus is on the role of transcription factors and signalling cascades, especially on the role of Pax6 gene, Wnt/β-catenin signalling pathway and their genetic interaction. A combination of gain-of-function (transgenic) and loss-of-function (conditional knock-outs) approaches is used. Our second main interest is eye evolution. Early morphological studies have suggested that eye has evolved multiple times during the course of evolution. In contrast, more recent genetic data indicate a conserved role of Pax6 and some other transcription factors in eye formation in a wide range of animals. In fact, eye assembly always relies on the same basic principle, i.e. photoreceptors located in the vicinity of dark shielding pigment. Several model systems including amphioxus, scallop, medaka and jellyfish are used in the laboratory to study various aspects of eye evolution.
The research programme of the laboratory aims to identify genes and molecular mechanisms involved in control of immune response and susceptibility to complex infectious diseases. We focus on complex diseases because they are responsible for the largest part of human morbidity and mortality and their genetic analysis is subject of an intensive international effort. They are controlled by multiple genes and hence their pathogenesis cannot be explained by effects of a single gene with omission of others. Leishmaniasis is such a complex disease and it has served as a major paradigm of immune response to an infectious agent. We aim to identify the genes and functions controlling this disease. The disease is caused by protozoan parasites of genus *Leishmania* that multiply in macrophages. Different species of *Leishmania* induce different symptoms, but even the patients infected by the same species develop different clinical manifestations. Many phenomena observed in human leishmaniases can be investigated in *Leishmania major* infection in mouse. Our approach uses a combination of genetic dissection with screening of a large set of immunological and clinical parameters of the disease. We mapped 21 *Lmr* (*Leishmania major* response) loci and found that gene effects on disease symptoms were organ-specific and heterogeneous. These 21 individual *Lmr* loci control 17 different combinations of pathological and immunological symptoms. Eight loci control both organ pathology and immunological parameters and 13 only immune reactions. Fifteen *Lmr* loci are involved in one or more genetic interactions showing that gene interactions are common in response to *L. major*. Moreover, parasite elimination, immunological and pathological processes are regulated independently. In conclusion, these studies revealed a network-like complexity of the combined effects of the multiple functionally diverse QTLs (quantitative trait loci). *Lmr* loci are likely relevant also for other diseases. Interestingly, nine of ten *Lmr* that influence serum IgE level after *Leishmania major* infection were mapped in the regions homologous with the human chromosomal segments that control total serum IgE in human atopic diseases. However, for the Lmr9 locus, the homologous human regions have not been connected with atopy. Thus, this locus may point to hitherto undetected human genes that are relevant for atopy. Indeed, in the position homologous to Lmr9 on chromosome 8q12 we demonstrated a novel human IgE-controlling locus. This finding shows precision and predictive power of mouse models in investigation of complex traits in humans.

**Fig. 2.** *Leishmania* parasites in macrophage.

**Fig. 3.** *Leishmania* stained with propidium iodide and LDS 751.

**Fig. 1.** Cutaneous leishmaniasis.


As a long-term research programme of our laboratory we have been investigating the mechanisms by which tumour cells are capable to escape from immune responses. Our projects are focused on regulation of genes encoding molecules crucial for antigen presentation and for tumour cell elimination by specific immune responses, on mechanisms of immunosuppression and its possible overcoming, and, finally, on experimental anti-tumour immunotherapy. Most of our studies employ murine models for tumours associated with human papilloma virus [aetiological agent of the cervical carcinoma]. Special attention has been paid to the setting of the minimal residual tumour disease treatment after primary tumour resection or chemotherapy.

MHC class I deficiency on tumour cells is a frequent mechanisms by which tumour cells can escape from specific immune responses. We have been interested in mechanisms underlying reversible MHC class I downregulation on tumour cells. We have found that epigenetic agents induce expression of genes involved in antigen-processing machinery and surface expression of MHC class I molecules on tumour cells, as well as of selected co-stimulatory and co-inhibitory molecules. Further analysis revealed that MHC class I downregulation in our model cell lines was associated with epigenetic silencing of antigen-presenting machinery genes. Our current projects in this field are focused on in vivo experiments with the aim to optimize immunotherapy of MHC class I-deficient tumours combined with administration of DNA methyltransferase inhibitors. We are also interested in epigenetic mechanisms underlying regulation of genes encoding antigen-presentation machinery genes, as well as co-stimulatory/inhibitory genes in antigen-presenting or regulatory immunocytes.

Our next areas of interest are populations of immunoregulatory cells (NKT, T-regulatory and myeloid-derived suppressor cells) and their dynamics in the course of tumour growth and therapy, as well as their mutual interactions. Recently, we have shown that administration of a glycolipid ligand activating NKT cells, β-galactosylceramide, inhibited growth of recurrent MHC class I-positive and -deficient tumours after surgery. Along with these projects we have been interested in experimental anti-tumour immunotherapy and vaccines. We have been investigating the impacts of several chemotherapeutic agents on anti-tumour immunity and on regulatory cell populations. We have used cell and gene therapy approaches and dendritic cell-based vaccines, as well as genetically modified tumour cells producing cytokines [especially IL-12-producing cells] for vaccination and immunotherapy optimization.

**Fig. 1.** ELISPOT (Enzyme-linked immunosorbent spot) analysis of the spleen cell activation with a ligand for NKT T-cell receptor (C12 β-D-GalactosylCeramide) and its inhibition with the anti-C10d-antibody demonstrates that the C12 β-D-GalactosylCeramide effects are mediated through its presentation by the C10d molecules. Each colour spot represents one interferon-γ-producing spleen cell.

**Fig. 2.** Tumour growth curves in control mice and mice subjected to chemio- and immunotherapy and their combination. Tumour inhibitory effects of combined epigenetic agents, 5-azacytidine (5AC) and immune activator unmethylated oligodeoxynucleotide (CpG 1826). MHC class I-deficient tumour cells were transplanted on day 0. In experimental groups, 5AC was repeatedly administered on days 7, 10, 14, 17, 21, 24, 28; immune activator, CpG 1826 was administered on days 3 and 10. Significant inhibition was observed in all treated mice, as compared to the untreated controls. Combined therapy was significantly more effective as compared to monotherapies only.
Our laboratory carries out structural studies on various proteins of biological or medicinal interest using protein crystallography. Among our targets, proteases from pathogenic organisms [2-4], antibody fragments as well as other human enzymes [1] take a prominent position.

HIV protease (HIV PR) research is focused on development of novel potent inhibitors as well as on understanding the structural basis of drug resistance. More than two decades into the global HIV epidemic, HIV PR still remains an attractive target for structure-based rational drug design. Although nine inhibitors targeting HIV PR are currently approved for clinical use, their therapeutic efficiency is hampered mostly by resistance development. Understanding PR resistance at the structural level and development of new PI acting by an alternative mode of inhibition is thus essential for successful treatment of HIV-positive patients. Our recent contribution to the field comprises structural studies of the enzyme–inhibitor complexes [2, 3]. Several recombinant antibody fragments of potential diagnostic and/or immunotherapeutic use (e.g. against human carbonic anhydrase IX, CD44, and CD3) have been prepared and characterized in our laboratory with the aim to improve their radionuclide labelling or to introduce further useful properties.
From left:
Pavlína Rezačová, PhD / Head of Laboratory
Jiří Brynda, PhD / Research Fellow
Magdalena Hafajž, PhD / Research Assistant
Pavel Mader, MSc / PhD Student
Pavel Těšínský, MSc / PhD Student (since 2010)
Jana Pisačková / Diploma Student
Věra Mrkvičková / Technician
Irena Siegllová, MSc / Research Assistant
Milan Fabij, PhD / Research Fellow
Jana Sedláčková, DSc / Research Fellow
Jitka Krejčiová / Technician

Not on the picture:
Jan Konvalínka, Assoc Prof, PhD / Research Fellow
Václavík Král, PhD / Research Fellow
David Krejčí, MSc / Research Assistant
Petr Pachl, MSc / PhD Student
Veronika Krejčíková, MSc / PhD Student (until 2009)
Tereza Vávříková / Diploma Student
Our work is focused on proteinases, especially metalloproteinases that process extracellular matrix (ECM) proteins or release [shed] ligands and their receptors from the cell surface. Interactions between cells and matrix control cell differentiation, survival, migration, and activation via cell surface receptors and adhesion molecules. Especially adhesion molecules sense changes in the composition of extracellular matrix that is affected by proteinases and their inhibitors. Balance between these two molecule classes determines if tissues and organ architecture are to be built up or disrupted. Thus, this balance is pivotal for tissue homeostasis and disturbance may lead to development of various pathologies such as cancer, chronic inflammation, or fibrosis.

Our research activities focus on how proteinases process ECM-proteins and how these changed matrix proteins (i.e., their fragments) affect the biology of various cell types. These investigations are focused specifically on several research areas: epithelium/epidermis and currently also liver and colon pathogenesis. Inflammatory reactions in these tissues are of our special interest as regulated proteolytic activity in the epidermis and many epithelia is crucial not only to maintenance of the body and organ barriers, but also to regulation of local inflammatory reactions. For instance, we are currently analysing the impact of matrix metalloproteinases 19 and 28 on development of colitis in DSS-induced model using MMP-19- and MMP-28-deficient mice. The exacerbation of the colitis in the knockout mice together with elevated concentrations of pro-inflammatory cytokines derived from colonic tissue suggests that MMP-19 has a role in maintenance of intestinal homeostasis. According to these results we propose a protective effect of MMP-19 during colitis.

To understand development and progression of liver fibrosis and inflammation processes, our research in this area analyses the effects and consequences of metalloproteinase-mediated turnover of extracellular matrix and the release of regulatory molecules from the cellular surfaces, a process that is mediated by shedding proteinases.

### References

Our long-term interest is to determine how cells decode information stored in the genome. Information in DNA is fragmented and we study processes and complexes that splice these fragments together and generate meaningful information that is further translated into amino acid sequence in a protein. We focus on molecules called RNAs that serve as a courier between DNA and proteins. However, it appears that RNA does not act as a simple "messenger" but undergoes various changes that significantly change information it carries. Our major aim is to analyse the process called RNA splicing and we mainly focus on variations in splicing among different cells and on assembly of the machinery that catalyses RNA splicing. We also aim to determine why mutations in the splicing machinery cause retinitis pigmentosa, a human genetic disease characterized by photoreceptor cell degeneration. As we study all these interesting processes directly in living cells, we widely employ advanced microscopy techniques (e.g., live cell imaging, FRET, FCS).

The zygotic genome activation is the first step in the execution of the genome-encoded program that forms a new organism from a single fertilized cell and it is an essential event in the life of every sexually reproducing organism. The zygotic genome activation is closely associated with formation of pluripotency, i.e. the ability of cells to differentiate into any body cell type. Pluripotency is most studied in two artificial cell types, which maintain pluripotency during in vitro culture: embryonic stem cells (ESCs), which are derived from the inner cell mass of the blastocyst, and induced pluripotent stem cells (iPSCs), which form upon reprogramming gene expression in somatic cells with specific pluripotency factors that include transcription factors from the core transcription factor network controlling ESC renewal and pluripotency. A similar network forms in a stepwise manner during the mouse zygotic genome activation, which initiates at the early two-cell stage.

We study reprogramming of oocytes into pluripotent blastomeres of an early embryo [oocyte-to-embryo transition]. This model is the natural parallel to the artificial reprogramming of somatic cells into iPSCs. The oocyte-to-embryo transition, however, is distinct. It is a unidirectional transient process executed by cytoplasmic factors, as demonstrated by animal cloning by nuclear transfer. Our primary research interest is in post-transcriptional mechanisms underlying oocyte-to-embryo transition. These mechanisms include control of maternal mRNA stability, small regulatory RNAs in miRNA and RNAi pathways, and production of maternal transcription factors, which will control gene expression in the embryo. Our goal is to understand how control of gene expression creates developmental competence in vivo. Research of pluripotency is eminent for medicine and biotechnology where pluripotency plays a role in an ever-growing number of applications. Understanding control of the oocyte-to-embryo transition will provide original insights into stem cell biology and will likely contribute to efficient and safe production of pluripotent stem cells, efficient cloning technologies, informative prenatal diagnostics, and understanding of pathology of sterility and developmental defects.

**Methods**


**Funding**

- EMBO, 1483 – EMBO Installation Grant, 2007–2011, P. Svoboda
- GA DR, GAP305/10/2215 – Control of chromatin and pluripotency by microRNAs, 2010–2013, P. Svoboda
From left:
Matyáš Flemr, MSc / PhD Student
Katerina Chalupnikova, PhD / Research Fellow
Kateřina Podolská, MSc / PhD Student
Radek Malík, MB, PhD / Research Fellow
Petří Svozová, PhD / Head of Laboratory
Natálie Matiješčuková / Diploma Student [since 2010]

Not on the picture:
Jana Nejedínská, MSc / PhD Student
Lenka Sarnová / Diploma Student [until 2010]
Our laboratory was amongst the first to complete genome projects. Information generated in these projects was used in evolutionary studies and recently also in biotechnological applications. Using the 454 next-generation sequencing facility (GS FLX/Titanium), we characterize genomes of different species and metagenomic samples. To understand the evolution of eukaryotes and the developmental processes that they regulate, it is necessary to analyze their genomes. Single-cell eukaryotes with their branching close to the root of the evolutionary tree are the best candidates for genome studies. The availability of the genome sequences will allow inferences to be made about the gene complement of the common eukaryotic ancestor. The genome projects under way are those of *Mastigamoeba balamuthi* and *Diplonema papillatum*. The metagenomic analyses of environmental samples and unculturable microbes are under way, too.

A second major project of our group is directed towards identification of markers specific for head and neck cancer tissue with potential applications in medical diagnosis. We use the Illumina microarray chip technique for detection of appropriate gene sets that are upregulated in this cancer disease. The found markers could identify the disease subtype and so help to aim the treatment.

---

**Fig. 1.** Graphical presentation of differences in expression of genes. The samples have been taken from head and neck squamous cell cancer patients with and without human papilloma virus infection.

**Fig. 2.** Tissue-specific expression pattern of *csSilk7/5A* transcription factor visualized (dark violet) by whole-mount in situ hybridization of adult jellyfish *Craspedacusta sowerbyi* [freshwater hydrozoan crinarian]. Expression is localized in gonads (germ cells, production of oocytes) and at the margin of manubrium (nerve cells – mechanosensors, feeding).

**Fig. 3.** Next-generation sequencer GS FLX (Roche).
From left:
Jan Pačes, PhD / Research Fellow
Václav Pačes, Prof, DSc / Research Fellow
Hynek Bína, PhD / Research Fellow
Michal Kolář, PhD / Research Fellow
Šárka Pinkasová / Technician
Čestmír Vlček, PhD / Head of Laboratory
Miluše Hrudařová, MSc / PhD Student
Monika Muyterová / Bachelor Student (since 2010)
Jakub Rídl, MSc / PhD Student

Not on the picture:
Barbora Dvořánková, PhD / Research Fellow (since 2010)
Mária Džunková / Diploma Student (until 2010)
Petra Feglarová, MSc / PhD Student (since 2010)
Jan Fousek, PhD / Research Fellow
Zdeněk Krejčík, MSc / PhD Student (since 2010)
Pavol Szabo, MSc / PhD Student
Jana Šachová, MSc / PhD Student [maternity leave]
Markéta Urbanová, MD / PhD Student (maternity leave)
Petr Vojta / Diploma Student (until 2009)
Lenka Záveská Drábková, PhD / Research Fellow
The IT department provides a range of information technology services to support various needs within the Institute. The main tasks include the administration of LAN and wireless network in the domain img.cas.cz, administration of institutional servers (DNS, mail, web) and storage area network (SAN) infrastructure, and performing data backup and archiving. The critical information technology equipment is housed in modern data centre rooms with controlled air-conditioning, uninterrupted power supply, temperature and humidity monitoring, and a fire protection system. The network security is assured by a firewall appliance that allows secure remote access to the computer network (VPN) and anti-spam plus anti-virus solutions, both on the server side and on the user computers. On a daily basis, the IT department ensures the installation and registration of computers and printers to the computer network, hardware purchase and consultancy, and support to users of Windows and Macintosh platforms. For commonly used software at the Institute, the volume and site licensing options are negotiated. Special support is provided to other technical and scientific departments, e.g. developing simple websites and on-line tools, maintaining dedicated databases, such as animal tracking system. The IT department also operates the audio-visual equipment in the conference hall and provides computers for courses and conferences organized at the Institute.
The facility was established in late 2005 after the purchase of the Affymetrix GeneChip System and was initially operated by the staff from the Laboratory of Mouse Molecular Genetics. Since January 2007, it has become an independent unit which provides full chip microarray services, real-time quantitative PCR service and high-throughput methods using the robotic equipment. The services are provided not only to the research groups at the Institute of Molecular Genetics, but also to other academic institutions in the Czech Republic as well as abroad. The core facility is equipped with two microarray platforms: Affymetrix GeneChip System and Illumina BeadStation 500, real-time PCR cycler Roche LC480, JANUS robots and EnVision Plate Reader from PerkinElmer, and also with instruments for assessment of quality and quantity of processed samples (spectrophotometer Nanodrop and capillary electrophoresis Agilent Bioanalyzer 2100). The facility represents one of the European certified Affymetrix core labs.
Monoclonal Antibodies and Cryobank

Dobromila Matějková
dobromila.matejkova@img.cas.cz

Monoclonal Antibodies Facility
The facility provides preparation of mouse monoclonal antibodies including immunization using a particular immunization protocol, ELISA testing of production of specific antibodies, cloning of selected samples, freezing of cryobank samples, cultivation of cell culture supernatants, or preparation of ascitic fluid from selected clones and isotype determination of the produced antibody. Further services comprise testing of cell culture supernatants for the presence of mycoplasmas and freezing of cell line banks and hybridomas.

Cryobank
The cryobank serves for long-term storage of samples in liquid nitrogen. The current cryobank capacity is 320,000 samples, with further possible extension. The cryobank stores cell lines, hybridomas, mouse sperm and mouse embryos in liquid nitrogen or its vapours. The storage containers (LABS40K - Taylor-Wharton and 24K) are connected to the exterior liquid nitrogen container for 6,000 litres and supplied automatically. The entire cryobank system is secured by a backup energy source in case of power failure. All operations, diagnostics and monitoring of the level of liquid nitrogen in the storage containers are fully automated and controlled. Parameters (temperature, humidity, O₂ concentration) and safety both in the cryobank and in the individual storage containers are followed by the monitoring system with GSM and web interface outputs.
Flow Cytometry and Light Microscopy

Ondrej Horváth
ondrej.horvath@img.cas.cz

The facility provides methodological and instrumentation background for flow cytometric and fluorescence microscopy techniques. At present, the facility is equipped with two cytometers – BD FACSCalibur and BD LSRII. The LSRII instrument is a four-laser [405, 488, 561 and 633-nm] instrument with 14 fluorescence detectors. A large set of dichroic mirrors and bandpass filters are available in the laboratory, making this instrument very flexible and capable to cover most of the flow cytometry applications. Both cytometers are equipped with the HTS loader for high-throughput analysis of samples directly from 96- or 384-well plates. The facility is also equipped with an AutoMACS Pro (Miltenyi Biotec) magnetic separator for automatic rapid sorting of cells, as well as cell culture facilities. The facility is running three microscopes: laser scanning confocal microscope with superfast scanner (Leica TCS SP5 AOBS TANDEM), Leica inverted fluorescent microscope with TIRF illumination (Leica), wide-field inverted fluorescence microscope with laser photomanipulation (DeltaVision Core). This state-of-art instrumentation allows facility users to use a wide range of microscopy techniques including FRET, FRAP, time-lapse experiments, membrane studies, vesicle transport studies, etc. Several offline analysis workstations are also available in the facility, for analysis of flow cytometric [FlowJo] and image data [SoftWorx Suite, Imaris, LAS AF, Huygens, ImageJ]. In the near future the laboratory will be equipped with a high-speed cell sorter.
The service unit offers preparation of tissue culture media and solutions (ranging from redistilled deionized water and PBS through media such as RPMI, MEM varieties, HBSS, trypsin, to custom-made solutions), preparation of bacteriology media and plates (clear and with selection agents), sterilization of solutions and material (steam sterilization, filtration of various grades), distribution of FBS, transfection agents, glass and plastic washing, decontamination of GMO and other hazardous waste (annual volume about 5,000 kg), organization of working cloth washing (more than 4,000 items per year).
Genetically modified mouse models have become a key tool in basic and biomedical research. The ability to engineer the mouse genome has greatly transformed biomedical research in the last decade. Crucial for this technology is the ability to control the expression of genes of interest. It is possible to increase or decrease gene expression, or eliminate the expression of a gene completely. Transgenic and gene knock-out/knock-in technologies have become important experimental tools for assigning functions to genes at the level of whole complexity of organism, creating models of genetic disorders, evaluating effects of potential therapeutic targets and drugs, and thus helping to answer fundamental issues in basic and applied research.

The Transgenic Unit at the Institute of Molecular Genetics (TgU) was established under the direction of Assoc Prof Radislav Sedláček in 2008/2009 to offer the research community at IMG and other cooperating institutions the opportunity to study the function of individual genes using mouse models. Our services include pronuclear microinjection of DNA constructs into mouse zygotes for the production of transgenic founders; microinjection of targeted ES cell lines into morulas (8-stage cell embryo) to produce chimeric mice; mouse archiving (cryopreservation of embryos and sperm); and recovery of live mice from cryopreserved embryos and sperm, analysis of sperm viability, re-derivation of mouse strains and lines, and others (see also our web page at http://tgunit.img.cas.cz/). We also provide consultation and assistance services, and information on the design and use of genetically modified transgenic mice. All of our services are also available to external institutions and researches irrespective whether they are from academic or profit
From left:
Sandra Potyšová, MSc [since 2010]
Radoslav Sedláček, Assoc Prof, PhD / Head
Veronika Libová, MSc [since 2009]
Inken Maria Beck, PhD

Not on the picture:
Irena Placerová, MSc
Lenka Michalčíková, MSc [until 2010]
Jana Ježková, MSc [until 2009]
Animal Facility (Mice)

Jan Honetschläger
jan.honetschlager@img.cas.cz

The IMG animal (mouse) facility has recently been housed in three buildings on the Krč campus and is accredited for work with genetically modified animals, with total capacity up to 8,000 cages. To date, we have available about 160 mouse strains; most of them are unique. All animals are housed under standard pathogen-free conditions required for high-quality research. We built a new quarantine with a capacity up to 400 cages, allowing us to import animals from cooperating institutes more easily. The animal facility also hosts the Transgenic Unit, which produces various types of transgenic and gene knock-out mice and performs re-derivation from the quarantine. Another building of the animal facility that was renovated in 2010 accommodates the experimental space for poultry. It also houses instruments for X-ray irradiation and sonography, both available to the entire Campus of Biomedical Institutes of the Academy of Sciences.
Animal Facility (Chicken)

Martina Ješátková
martina.jesatkova@img.cas.cz

This facility is located in the village Koleč, north of Prague, about 45 km from the main Campus of Biomedical Institutes in Prague-Krč. It mainly takes care of breeding genetically defined inbred, congenic and outbred chicken lines (and one duck line). The facility produces eggs, embryos and chickens for several research groups focusing on chicken models. Until the experimental laboratories for work with chicken are reconstructed on the Prague-Krč Campus, the facility is also used for experimental laboratory work.
From left: Petra Faloutová, Jaroslava Smadelová, Martina Jedličková, MSc / Head, Jitka Dvořáková, Alena Eisensteinová, Radmila Slíková, Alena Porazilová, Miloslava Vilhelmová, PhD

Not on the picture: Eva Bernášková, Ladislava Hachová (until 2010), Zdeňka Koptlová, Kamila Thunová, Miroslav Vaverková (until 2009), Jaroslav Vlasíková.
Building Maintenance

Miroslav Heyduk
miroslav.heyduk@img.cas.cz

Entrance hall
Milan Haláš Auditorium
Central staircase
Cafeteria
Meeting point
View from the park
Office of the Director

Šárka Takáčová
sarka.takacova@img.cas.cz

From left:
Kateřina Sedláčková
Leona Krausová
Šárka Takáčová, MSc / Head
Gabriela Marešová
Zdeňka Schuhová
Jiří Jonák, Prof, MD, DSc
Finances and Administration

Renata Schönová
renata.schonova@img.cas.cz
The BIOCEV division of IMG was established in September 2009. Its main task is to ensure, in terms of organization, the preparation and implementation of the project of a new research centre - Biotechnology and Biomedicine Centre of Academy of Sciences and Charles University in Vestec – BIOCEV. BIOCEV is a joint project of six institutes of the Academy of Sciences of the Czech Republic (Institute of Molecular Genetics, Institute of Microbiology, Institute of Physiology, Institute of Experimental Medicine, Institute of Biotechnology, and Institute of Macromolecular Chemistry) and Charles University in Prague, represented here by two faculties (Faculty of Science and First Faculty of Medicine), and is prepared with the ambition of creating a European centre of excellence. The project builds upon three pillars of the knowledge triangle. The research programme, which provides scientific outputs of highest quality, stands above all. It involves five fundamental areas: Functional Genomics, Cellular Biology and Virology, Structural Biology and Protein Engineering, Biomaterials and Tissue Engineering, and Development of Diagnostic and Therapeutic Procedures. This scientific programme will be supported by several top-quality core facilities.

Transfer of research results into practice represents the second pillar of BIOCEV. The centre will focus on intensive collaboration with the commercial sphere and will support preservation of intellectual property and its further utilization. The third pillar is teaching and education namely of PhD students, which will be achieved within current study programmes of Charles University and by newly accredited programmes in biotechnology and biomedicine. In addition, BIOCEV will organize and facilitate specialized international courses for Czech and international students and young scientists. The new centre will also offer training of business employees in advanced biotechnology methods.

BIOCEV has entered two networks of European consortia of ESFRI (European Strategy Forum on Research Infrastructures) – EuroBioImaging and INFRAFRONTIER. This integration into the European Research Area even before establishment of BIOCEV itself marks the quality of the future research centre. The new centre will be built in the municipality of Vestec, Central Bohemia and will accommodate up to 600 employees and 250 Master and PhD students. Estimated costs for construction amount to 92 mil EUR. Funding will be provided by the European Regional Development Fund within the Operational Programme Research and Development for Innovations. The construction should start in the middle of 2011, its operation then late in 2013. For more information visit http://www.biocev.eu/.
From left:
Romana Maštalířová, MSc [since 2009]
Jan Rajnoch, MD / Head
Ivana Sýkorová, PhD [since 2009]
Božena Šléglová [since 2010]

Not on the picture:
Jana Bartušková, MA (02-07/2010)
Council of the IMG

The Council of the Institute serves as an advisory authority to the Director and decides on essential scientific and organizational issues. Its members are appointed by election.
The main task of the Supervisory Board is to monitor the financial and legal matters connected with the Institute administration. Its members have been selected by the Academy of Sciences from Academy and business sphere representatives.
ANDĚRA


BARTEK


BARTŮNĚK


BLAHOŠ


VLČEK


OTHER PUBLICATIONS UNDER IMG AFFILIATION (from former groups or core facilities)


29/01/09 Tobias Dietschy
(Dualsystems Biotech AG, Schlieren, Switzerland)

16/03/09 David Klatzmann
(Immunology-Immunopathology-Immunotherapy at Pitié-Salpêtrière hospital, UPMC, Paris, France)

01/04/09 Christian Dahmann
(Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany)

07/04/09 Serkan Ismail Gökçuna
(Technical University of Munich, Munich, Germany)

20/04/09 Arthur Weiss
(Howard Hughes Medical Institute, University of California, San Francisco, CA, USA)

21/05/09 Solomon H. Snyder
(Johns Hopkins Medical School, Baltimore, MD, USA)

18/06/09 Krzysztof Szyfter
(Department of Environmental Mutagenesis, Institute of Human Genetics of the Polish Academy of Sciences, Poznan, Poland)

25/06/09 Masahiko Harata
(Department of Molecular and Cell Biology, Graduate School of Agricultural Science, Tohoku University, Japan)
09/11/09  **Jeffrey Good**  
[Department of Evolutionary Genetics, Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany]

06/10/09  **Olivier Cuvillier**  
[Sphingolipids & Cancer Research Laboratory, INSERM, Toulouse, France]

21/10/09  **Jonathan C. Howard**  
(Institute for Genetics, University of Cologne, Cologne, Germany)

26/10/09  **David Margolis**  
[Michael Hooker Research Center, University of North Carolina at Chapel Hill, NC, USA]

01/09/09  **Harry F. Noller**  
[Center for Molecular Biology of RNA, University of California, Santa Cruz, CA, USA]

22/09/09  **Vladimir Varga**  
[Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany]
03/02/10 Cheng Zhu
(Institute for Bioengineering and Bioscience, Georgia Institute of Technology, Atlanta, GA, USA)

12/02/10 Shazib Pervaiz
(National University of Singapore, Singapore)

03/03/10 Wolfgang Zachariae
(Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany)

07/04/10 Kanagaraj Radhakrishnan
(Institute of Molecular Cancer Research, University of Zurich, Switzerland)

28/04/10 Petko Petkov
(The Jackson Laboratory, Bar Harbor, ME, USA)

26/05/10 Jonathon Howard
(Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany)

11/06/10 Anatoly Ruvinsky
(Institute for Genetics and Bioinformatics, University of New England, Armidale, Australia)
01/12/10  **Andreas Ludwig**  
(Research Group for Vascular Pharmacology, Institute of Pharmacology and Toxicology, RWTH Aachen University, Aachen, Germany)

09/12/10  **Karina Reiß**  
(Department of Dermatology and Allergology, University Hospital Schleswig-Holstein, Kiel, Germany)

02/11/10  **Marion MacFarlane**  
(MRS Toxicology Unit, Leicester, England)

03/11/10  **Frank Buchholz**  
(Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany)

06/10/10  **Attila Mócsai**  
(Semmelweis University School of Medicine, Budapest, Hungary)

13/10/10  **Ken Jacobson**  
(Department of Cell and Developmental Biology, University of North Caroline, Chapel Hill, NC, USA)

18/10/10  **Kristijan Ramadan**  
(Institute of Veterinary Pharmacology and Toxicology, University of Zürich, Switzerland)

20/09/10  **André Veillette**  
(Institut de recherches cliniques de Montréal (IRCM) Montréal, Québec, Canada)

02/07/10  **Thomas Boehm**  
(Department of Developmental Immunology, Max Planck Institute of Immunobiology, Freiburg, Germany)
Highlights of 2009-2010

Organization & Development

Development of the Institute complex further advanced
Construction of the kindergarten with gym and of the new guest house was completed within 2010, and by the end of the year both facilities were ready for opening. Pavilion CH underwent a thorough reconstruction and is now housing the non-mouse (mainly chicken) experimental animal facility.

New instruments
In 2010 we started operation of a new histology unit equipped with Tissue processor Leica ASP200S, Paraffin embedding station Leica EG1150H and Microtome RM2255 (operated by the group of Vladimír Kořínek). In pavilion CH a new orthovoltage X-ray instrument T-200 (Wolf-Medizintechnik) for regulated radiation of cells and mice was installed. The mouse animal facility of the Institute was equipped with new individually ventilated breeding cages.

New division
A new division of IMG was established in 2009 with the aim to support preparation and organization of project BIOCEV (Biotechnology and Biomedicine Centre of The Academy of Sciences and Charles University) in Vestec near Prague, a joint project of six institutes of the Academy of Sciences of the Czech Republic [Institute of Molecular Genetics, Institute of Biotechnology, Institute of Microbiology, Institute of Physiology, Institute of Experimental Medicine, and Institute of Macromolecular Chemistry] and two faculties of Charles University in Prague [Faculty of Science and First Faculty of Medicine], whose application was completed and sent to the European Commission for approval at the end of 2010. Further information can be found at http://www.biocev.eu/.
Awards & Honours

2009

Jiří Forejt – Prize of the Minister of Education, Youth and Sports of the Czech Republic for outstanding results in research, experimental development and innovations for 2009
Laboratory of Jiří Forejt (Zdeněk Trachtulec, Soňa Gregorová, Petr Jansa, David Homolka, Ondřej Mihola) – Prize of the Academy of Sciences of the Czech Republic
Ondřej Ballek – Prize for the best diploma thesis awarded by the Dean of Charles University, Prague
Daniel Smrž (and the Laboratory of Petr Dráber) – Prize of the Czech Immunological Society for the best paper by a young immunologist in 2008
Petr Heneberg – Bolzano Award awarded by the Rector of Charles University, Prague
Václav Hořejší – The Sir Hans Krebs Lecture and Medal awarded by FEBS
Daniel Smrž – Award of the Czech Society for Analytical Cytology
Jiří Bartek – The Shay Shacknai Prize for Cancer Research, Hebrew University of Jerusalem; Medal of the Faculty of Medicine, Charles University

2010

Ondřej Mihola – Arnold Beckman Prize for the best publication in the field of genetics, Beckman Coulter CR and the Czech Society for Biochemistry and Molecular Biology
Václav Pačes – Medal of Emil Votoček awarded by the Institute of Chemical Technology, Prague
Ondřej Mihola – Scopus Award for year 2009 awarded by the prominent scientific publisher Elsevier BV
Martina Huranová – Josef Hlávka Award for the best students and young talented researchers by the Hlávka Foundation
Jan Svožoda – National Prize of the Czech Government “Česká hlava” (Czech Brains)
Jiří Bartek – Neuron 2010 for life-long merits in medicine awarded by Karel Janeček Foundation
Highlights of 2009-2010

Seminars & Conferences Organized/Co-organized by IMG

Most of these events were held in the new conference hall of IMG named after the founder of the Institute “Milan Hašek Auditorium”.

Conferences:

<table>
<thead>
<tr>
<th>Year</th>
<th>Date</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>05/06</td>
<td>2nd IMG PhD Conference</td>
</tr>
<tr>
<td></td>
<td>01-03/10</td>
<td>EMBO Workshop on Mitochondria, Apoptosis and Cancer (keynote lecture by Guido Kroemer, INSERM, Villejuif, France)</td>
</tr>
<tr>
<td></td>
<td>11/12</td>
<td>Annual IMG Conference</td>
</tr>
<tr>
<td>2010</td>
<td>25-28/03</td>
<td>T-cell Activation &amp; Technologies</td>
</tr>
<tr>
<td></td>
<td>29/04-05/05</td>
<td>Centennial Retrovirus Meeting [keynote lecture by David Baltimore, California Institute of Technology, Pasadena, USA]</td>
</tr>
<tr>
<td></td>
<td>20-21/05</td>
<td>ECBS 2010 Prague – The Second European Chemical Biology Symposium [keynote lecture by James Inglese, NIH, Bethesda, USA]</td>
</tr>
<tr>
<td></td>
<td>04/06</td>
<td>3rd IMG PhD Conference</td>
</tr>
<tr>
<td></td>
<td>08-10/06</td>
<td>EMBO Young Scientists Forum</td>
</tr>
<tr>
<td></td>
<td>01-04/09</td>
<td>52nd Symposium of the Society for Histochemistry [The Robert Feulgen lecture by Stefan W. Hell, MPI, Göttingen, Germany]</td>
</tr>
<tr>
<td></td>
<td>17/12</td>
<td>Annual IMG Conference</td>
</tr>
</tbody>
</table>

Regular weekly Institute seminars – speakers:

<table>
<thead>
<tr>
<th>Year</th>
<th>Speakers</th>
</tr>
</thead>
</table>
A significant part of our scientific community is represented by about 100 PhD students (20% international from both EU and non-EU countries), who significantly influence the atmosphere at the Institute and strongly contribute to its scientific output. Therefore, one of our priorities is to offer an appealing PhD programme that will attract the best students and will provide them with high-quality training for a career in molecular, cell and developmental biology, immunology, genetics, and virology. The PhD programme and related topics are organized by the Committee for PhD Matters, which consists of four PIs [Dominik Filipp, Pavel Hozák, David Staněk, Petr Svoboda] and two student representatives [Martina Huranová and Pavel Vopálenský].

Students apply to the programme through an on-line application. In 2010, nineteen candidates were selected and invited for a PhD interview. Applicants gave short English presentations of thesis research and were briefly interviewed and ranked by a three-member committee. During the interview applicants also visited several laboratories and met with group-leaders in order to find the best match. At the end, thirteen PhD students were recruited via the PhD interview procedure in 2010.

There is a number of English courses taught by scientists from the Institute: Acquisition and Processing of the Image in Microscopy [one-week practical course organized by P. Hozák], Advances in Immunology [K. Drbal, D. Filipp, R. Špišek, P. Otáhal, T. Brdička, V. Hořejší], Advances in Molecular Biology and Genetics [two-week lecture course organized by J. Jonák and P. Svoboda], Basic Immunology [P. Otáhal, V. Hořejší], Epigenetics [P. Svoboda], Innate Immunity [D. Filipp] and RNA structure and Function [D. Staněk]. PhD students also actively participate in labmeetings, journal clubs, and institutional seminars. Students can also attend English language classes, which take place directly in the IMG building to save time of PhD students.

We also aim to foster extracurricular training of our PhD students. In 2010, we started a “Welcome Weekend” for new PhD students where they are provided with basic information about the Institute and the PhD programme. In 2010, the IMG also hosted the EMBO Young Scientists Forum, which provided a number of opportunities for PhD students for career development and networking. PhD students also organize annual IMG PhD conferences and already a third conference in a row took place on 4th June 2010. With eleven student talks, a keynote lecture given by Mirka Uhlířová [Junior Group Leader, University of Cologne] and career development talk presented by Jan Peychl [Light Microscopy Facility Leader, Max Planck Institute for Molecular Cell Biology and Genetics, Dresden], the conference brought together students and other researchers in an informal atmosphere and continued a nice tradition started in 2008.

Further information on PhD studies at the IMG can be found at [http://www.img.cas.cz/phd].
<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>Supervisor(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ballek Ondřej</td>
<td>Rack1 as a candidate protein involved in the regulation of translocation of Lck to lipid rafts</td>
<td>Dominik Filipp; Faculty of Science, Charles University, Prague</td>
</tr>
<tr>
<td>Černohorská Markéta</td>
<td>The role of JAK/STAT signalling pathway in cellular senescence</td>
<td>Zdeněk Hodný; Faculty of Science, Charles University, Prague</td>
</tr>
<tr>
<td>Dušková Pavlína</td>
<td>The role of DNA damage in chemically induced senescence</td>
<td>Zdeněk Hodný; Faculty of Science, Charles University, Prague</td>
</tr>
<tr>
<td>Dzúr-Gejdošová Mária</td>
<td>Regulation of gene expression on the model of mouse consomic strains</td>
<td>Jiří Forejt; Faculty of Science, Charles University, Prague</td>
</tr>
<tr>
<td>Flachs Petr</td>
<td>Construction of three congenic strains and their phenotypisation</td>
<td>Zdeněk Trachtulec; Faculty of Science, Charles University, Prague</td>
</tr>
<tr>
<td>Hejhal Tomáš</td>
<td>Epigenetic regulation of immunactive gene expression in tumour cells</td>
<td>Milan Reiniš; Faculty of Science, Charles University, Prague</td>
</tr>
<tr>
<td>Kopová Ivana</td>
<td>The role of sumoylation in premature chemically induced cellular senescence</td>
<td>Zdeněk Hodný; Faculty of Science, Charles University, Prague</td>
</tr>
<tr>
<td>Kotáb Jan</td>
<td>Integration preferences of avian sarcoma and leukosis viruses</td>
<td>Jiří Hejnar; Faculty of Science, Charles University, Prague</td>
</tr>
<tr>
<td>Kovářová Denisa</td>
<td>RNAi and reversion of Rous sarcoma virus-induced tumorigenesis</td>
<td>Jiří Hejnar, Kateřina Trejbalová; Faculty of Science, Charles University, Prague</td>
</tr>
<tr>
<td>Machyna Martin</td>
<td>Dual role of CD9 protein in mast cell activation</td>
<td>Petr Dráber; Faculty of Science, Charles University, Prague</td>
</tr>
<tr>
<td>Mayer Alexandra</td>
<td>Pathophysiological role of matrix metalloproteinase 19 in development of liver fibrosis</td>
<td>Radislav Sedláček; Faculty of Science, Charles University, Prague</td>
</tr>
<tr>
<td>Nevařil Leonard</td>
<td>TRAIL-induced apoptosis in populations of colon cancer cell lines under various cultivation conditions</td>
<td>Ladislav Anděra; Faculty of Science, Charles University, Prague</td>
</tr>
<tr>
<td>Plesníková Michaela</td>
<td>The separation, characterization and cultivation of limbal stem cells</td>
<td>Vladimír Holáň; Faculty of Science, Charles University, Prague</td>
</tr>
<tr>
<td>Sarnová Lenka</td>
<td>Transgenic RNAi in mouse oocytes</td>
<td>Petr Svoboda; Faculty of Science, Charles University, Prague</td>
</tr>
<tr>
<td>Slávik Branislav</td>
<td>Targeting of genes of interest via avian retroviral receptor Tvc</td>
<td>Radislav Sedláček; Faculty of Science, Charles University, Prague</td>
</tr>
<tr>
<td>Svoboda Ondřej</td>
<td>Cloning, expression and characterization of recombinant growth factors</td>
<td>Petr Bartůňek; Faculty of Science, Charles University, Prague</td>
</tr>
<tr>
<td>Svobodová Eliška</td>
<td>Immunomodulation properties of mesenchymal stem cells</td>
<td>Magdalena Krulová; Faculty of Science, Charles University, Prague</td>
</tr>
</tbody>
</table>
Auxt Miroslav  
De novo DNA methyltransferases in the silencing of retroviral vectors [Supervisors: Jiří Hejnar, Filip Šenigl; Faculty of Science, Charles University, Prague]

Dušková Eva  
Regulation of alternative splicing [Supervisor: David Staněk; Faculty of Science, Charles University, Prague]

Faltýsková Helena  
Experimental models of the stem cell transfers for therapeutic purposes [Supervisor: Magdalena Krulová; Faculty of Pharmacy, Charles University, Hradec Králové]

Chudičková Milada  
Recombinant congenic strains – model for biomedical research [Supervisor: Marie Lipoldová; Faculty of Biomedical Engineering, Czech Technical Institute, Prague]

John Václav  
Genes for hybrid sterility in mice: mapping of epistatic interactions [Supervisor: Jiří Forejt; Faculty of Science, Charles University, Prague]

Kašpárek Petr  
Generation of a transgenic mouse model to study biological role of KLK5 in epidermis [Supervisor: Radislav Sedláček; Faculty of Science, Charles University, Prague]

Marášek Pavel  
Function of paxillin complexes in cell nucleus [Supervisor: Pavel Hozák; Institute of Chemical Technology, Prague]

Pitule Pavel  
Comparative genomic prediction of novel transmembrane adaptor proteins and their expression analysis [Supervisor: Karel Drbal; Faculty of Science, Charles University, Prague]

Přistoupilová Anna  
Development of real-time PCR assay for detection of Amphibiocystidium ranae as a model approach for studying rhinosporidiosis [Supervisor: Jan Pačes; 1st Faculty of Medicine, Charles University, Prague]

Šíma Matyáš  
Genetic influence on Trypanosoma brucei brucei infection in mice [Supervisor: Marie Lipoldová; Faculty of Science, Charles University, Prague]

Šimíček Michal  
FcrRI and Kit signal to actin cytoskeleton via different pathways [Supervisor: Petr Dráber; Faculty of Science, Charles University, Prague]

Šulcová Jitka  
Analysis of candidate transmembrane adaptor proteins [Supervisor: Karel Drbal; Faculty of Science, Charles University, Prague]

Těšina Petr  
Structure and function of hPrp31 mutant in Retinitis pigmentosa [Supervisor: David Staněk; Faculty of Science, Charles University, Prague]

Vavrochová Tereza  
Expression and function of molecules of innate immune system in embryonic phagocytes [Supervisor: Dominik Filipp; Faculty of Science, Charles University, Prague]

Vonková Ivana  
Biochemical and functional characterization of a novel transmembrane adaptor protein Nvl [Supervisor: Tomáš Brdička; Faculty of Science, Charles University, Prague]
PhD Theses 2009

Gusareva Elena
Impact of genetic and environmental factors on development of atopy and allergic diseases in Czech and Russian populations [Supervisor: Marie Lipoldová; 3rd Faculty of Medicine, Charles University, Prague]

Ivánek Robert
DNA microarrays and bioinformatics in biomedical research [Supervisors: Jiří Forejt, Stanislav Kmoč; Faculty of Science, Charles University, Prague]

Krejčíříková Veronika
Structural studies of mouse galectin-4 [Supervisor: Jiří Brynda; Faculty of Science, Charles University, Prague]

Růžičková Jana
Eye evolution and development: an insight from jellyfish and mouse [Supervisor: Zbyněk Kozmík; Faculty of Science, Charles University, Prague]
Huranová Martina
Assembly and recycling of functional splicing complexes in vivo [Supervisor: David Staněk; Faculty of Science, Charles University, Prague]

Krejčík Zdeněk
Taurine-nitrogen utilized by bacteria: a diverse set of phenomena [Supervisor: Václav Pačes; Institute of Chemical Technology, Prague]

Mader Pavel
Structure, function and inhibition of human carbonic anhydrases [Supervisor: Jiří Brynda; 1st Faculty of Medicine, Charles University, Prague]

Manning Jasper
Epigenetic agents induce MHC class I surface expression on tumor cells and reexpress an aberrantly silent marker of myeloid neoplasms [Supervisor: Milan Reiniš; 1st Faculty of Medicine, Charles University, Prague]

Nováková Zora
Cytokine expression in chemically-induced senescence [Supervisor: Zdeněk Hodný; Faculty of Science, Charles University, Prague]

Sedlák David
Panels of steroid receptor reporter cell lines for compound profiling and development of selective ligands for oestrogen receptor α and β [Supervisor: Petr Bartůňek; Faculty of Science, Charles University, Prague]

Vopálenský Pavel
Evolution of photoreceptors [Supervisor: Zbyněk Kozmík; Faculty of Science, Charles University, Prague]
Teaching (Semestral Courses)

**Molecular Mechanisms of Apoptosis**, Faculty of Science, Charles University (Ladislav Anděra)

**Solving Macromolecular 3D Structures**, Faculty of Science, Charles University (Jiří Brynda, Pavlína Řezáčová)

**Molecular Modelling and Bioinformatics**, Institute of Chemical Technology (Jiří Brynda, Pavlína Řezáčová)

**Anti-tumour Immunity**, Faculty of Science, Charles University (Jan Bubeník)

**Immunology and Gene Therapy of Tumours**, 1st Faculty of Medicine, Charles University (Jan Bubeník)

**Structure and Function of Cytoskeleton**, Faculty of Science, Charles University (Pavel Dráber)

**Molecular Genetics of Mammalian Organism**, Faculty of Science, Charles University (Jiří Forejt)

**Regulatory Mechanisms of Immunity**, Faculty of Science, Charles University (Vladimír Holáň)

**Immunology**, Faculty of Science, Charles University (Václav Hořejší, Tomáš Brdička)

**Molecular Immunology**, Faculty of Science, Charles University (Karel Drbal)

**Advances in Immunology**, Faculty of Science, Charles University (Dominik Filipp, Karel Drbal, Pavel Otáhal, Tomáš Brdička, Radek Špišek, Václav Hořejší)

**Cell Nucleus and Gene Expression**, Faculty of Science, Charles University (Pavel Hozák)

**Transmission Electron Microscopy in Life Sciences**, Faculty of Science, Charles University, and Czechoslovak Microscopy Society (Pavel Hozák)

**Image Acquisition and Processing in Biomedical Microscopy**, Czechoslovak Microscopy Society (Pavel Hozák)

**Microscopy Immunodetection in Biomedicine**, Czechoslovak Microscopy Society (Pavel Hozák)

**Model Organisms in Developmental Biology**, Faculty of Science, Charles University (Zbyněk Kozmík)

**Advances in Immunology of Infectious Diseases, Molecular Mechanisms of Defence against Infection**, 3rd Faculty of Medicine, Charles University (Marie Lipoldová)
Advances in Molecular Immunology, 3rd Faculty of Medicine, Charles University (Marie Lipoldová)

Soluble Mediators in Immune System, 3rd Faculty of Medicine, Charles University (Jarmila Vojtišková)

Bioinformatics, Faculty of Science, Charles University (Jan Pačes, Jiří Vondrášek)

Bioinformatics, University of Perugia, Perugia, Italy (Jan Pačes)

Molecular Genetics, Institute of Chemical Technology (Václav Pačes)

Gene Engineering, Institute of Chemical Technology (Václav Pačes, Tomáš Ruml, Jan Pačes)

Molecular and Cellular Oncology, Faculty of Science, Charles University (Jan Svoboda, Jiří Hejnar)

RNA structure and Function, 1st Faculty of Medicine, Charles University (David Staněk)

Advanced Techniques in Fluorescence Microscopy, Practical Course, Institute of Molecular Genetics (David Staněk)

Epigenetics, Faculty of Science, Charles University (Petr Svoboda)

Developmental Biology, Faculty of Science, Charles University (Petr Svoboda)

Advances in Molecular Biology and Genetics, annual 2-week lecture course, Institute of Molecular Genetics (Jiří Jonák, Petr Svoboda)

Innate Immunity, Faculty of Science, Charles University (Dominik Filipp)

Pharmacology, 2nd Faculty of Medicine, Charles University, Prague and Faculty of Medicine, Charles University in Hradec Králové (Jaroslav Blahoš)

Molecular Pathology, Faculty of Science, Charles University (Vladimír Kořínek)

Gene Expression, 1st Faculty of Medicine, Charles University (Jiří Jonák)

Seminars Biological Oxidation, 1st Faculty of Medicine, Charles University (Jiří Jonák)
Institute of Molecular Genetics of the ASCR, v. v. i.
Videňská 1083
Prague 4, Czech Republic

Where We Are

Iletiště Ruzyně (airport) → Dejvická station → Muzeum station → Budějovická station → Ústavy Akademie věd station

Bus 119 → Metro A → Metro C → Bus 193

Iletiště Ruzyně (airport) → Institute of Molecular Genetics (Campus of the Academy of Sciences)

Cab → TAXI